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Abstract (poster session)

A phase 1, single ascending-dose study of AVI-6002, a combination of two PMOplus™ compounds with activity against ebolavirus

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Objective: Ebola hemorrhagic fever (EHF) is a rare human disease caused by ebolavirus, a filamentous single-stranded, negative-sense RNA virus of the family Filoviridae. No vaccine or established effective therapy is currently available for this catastrophic disease. AVI-6002 is an experimental combination of two phosphorodiamidate morpholino oligomers with positive charges (PMOplus™) that specifically target two viral messenger RNAs (mRNAs) encoding ebolavirus proteins. AVI-6002 has demonstrated evidence of protection against lethal infection in experimental mouse, guinea pig and non-human primate models of ebolavirus infection. The objective of this clinical study is to determine the safety, tolerability and pharmacokinetics of intravenous administration of AVI-6002 in healthy human subjects over a dose range predicted to cover a therapeutic dose. Methods: In this first-in-man study, 30 healthy male and female subjects between 18 and 50 years of age were enrolled in 6 dose escalation cohorts of 5 subjects each and received a single intravenous (IV) infusion of AVI-6002 (0.01, 0.1, 1.0, 3.0, 6.0 and 9.0 mg/kg) or matched placebo in a 4:1 ratio. Safety was monitored through adverse event collection, telemetry, oximetry and serial blood tests, urine tests and electrocardiograms. The study was overseen by an independent Data Safety Monitoring Board (DSMB). Results: No significant safety concerns arose upon review of blinded study data from the first 5 cohorts by the independent DSMB. While 14 of the first 25 subjects dosed experienced a variety adverse events such as headache (n=4), nausea (n=3) or fatigue (n=2), almost all were mild or moderate in severity. The only exception was one episode of severe hypertension, which was not considered related to study drug. No changes in kidney function related to study drug were observed. Conclusion: Preliminary results of this first-in-man phase 1 study suggest that single IV administrations of AVI-6002 are well-tolerated up to a dose level of 6 mg/kg. Follow-up of subjects enrolled in the 6th cohort (9 mg/kg) is ongoing. Final, unblinded safety and pharmacokinetic results for all subjects will be presented. ClinicalTrials.gov ID: NCT01353027. This work is being conducted under contract with the Department of Defense Joint Project Manager Transformational Medical Technologies.